PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:	Attorney Docket No.: 3110.03US02
Kuslich	Confirmation No.:
Application No.: 10/702,096	Examiner: Alvin Stewart
Filed: November 5, 2003	Group Art Unit: 3738

For: SEMI-BIOLOGICAL INTERVERTEBRAL DISC REPLACEMENT SYSTEM

DECLARATION PURSUANT TO 37 C.F.R. §1.132

I, Michael Mac Millan, M.D., declare under penalty of perjury that the following is true and correct to the best of my knowledge, information and belief:

1. I graduated from University of North Carolina, School of Medicine in 1980.
2. I am an Orthopedic Surgeon specializing in the treatment of spinal disorders.
3. I have read and understood United States Patent Application No. 10/702,096 to Kuslich. (the "Kuslich Application").
4. I have read and understood United States Patent Application No. 09/827,427 to Belef et al. (the "Belef Application").
5. The Kuslich application describes methods and devices that stimulate the interconnected growth of fibrous and/or cartilaginous tissue within the disc space in order to stabilize the spinal motion segment by promoting the growth of living natural tissue that mimics the mechanical characteristics of a natural disc.
6. The growth factors and other fill materials disclosed in the Belef Application are not capable of causing the late stage cellular differentiation which gives rise to fibrocartilaginous tissue growth. It is well known in the art that post-natal

fibrocartilaginous tissue growth and development is a relatively late stage transformation of an existing population of cells. The basic process of tissue development utilizes signals to cause an early, undeveloped cell to divide and create multiple, undifferentiated copies of itself. These early cells are still capable of further differentiation, but instead of being signaled by growth factors or molecular signaling, their subsequent differentiation is caused by environmental mechanical forces. Tensile forces would cause these cells to become fibrous, and compressive forces may cause them to convert to bone. Thus, fibrocartilaginous tissue arises in response to the mechanical environment and is not directly due to the effect of growth factors.

7. It is also well known in the art that certain synthetic fibers, such as for example, cotton, when placed in a vascularized environment incite an inflammatory reaction which results in a fibrous proliferation and hence the growth of fibrous tissue. Synthetic fibers are routinely used in reconstruction of the abdominal wall to promote fibrous ingrowth and healing. Synthetic fibers configured into a mesh provide a scaffolding which induces the fibrous reparative tissue to form a sheet like tissue structure for containment.

8. The Belef Application maintains that healing of the annulus is promoted by the nonporous filled bladder in the disc space. There are two well known and accepted reasons why a bladder situated within the disc would have little ability to promote annular healing. First, a significant amount of metabolic nutrition comes from diffusion within the disc itself. Disturbing the disc contents would decrease the nutrition available to the annulus for repair. Secondly, the annulus itself is

largely without the cells required to bring about a reparative process. Once it is broached there is no possibility of reconstructing a continuous structure, vertebra to vertebra, that could be construed as "substantial healing".

9. Further, nothing in the Belef application teaches or discloses that the fill material promotes any annular healing or tissue growth. In contrast, the Belef Application at Paragraph 64 states:

> "Alternatively, the bladder 12 may facilitate healing of an annulus fibrosis, for example, through which fissures and the like have developed. In addition to the nucleus pulposus removed from the interior region 94, any nucleus pulposus that has leaked through such fissures may be removed. In this embodiment, the bladder 12 is preferably substantially nonporous, thereby containing the nucleus pulposus within the bladder 12 while the annulus fibrosis 92 is given opportunity to heal. Preferably, the bladder 12 is bioabsorbable such that the bladder 12 is substantially absorbed by the patient's body after sufficient time for the annulus fibrosis to substantially heal. Thus, once healed, the patient's spinal disc may be restored to a substantially normal, healthy disc."

Thus, according to Belef, the fill material is not even in contact with the annulus during the healing process, much less promoting the growth of new tissue. In fact, Belef teaches that it is only after the annulus is healed that the bladder may be reabsorbed to expose the processed nucleus pulposus fill material.

10. Even if a "substantial healing" of the annulus did occur, such annular tissue is not the same as the fibrous and/or cartilaginous tissue that makes up the inner disc

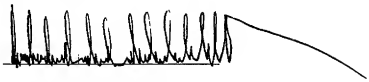
material. In contrast to inner disc tissue, annular tissue consists of overlapping fibrocartilaginous bands that consist of a particular collagen type known as Type I. Type I collagen is specifically generated to resist tensile forces, such as those seen in the annulus fibrosus. In contrast to the annular collagen, the collagen formed by the inner portion of disc tends to be predominantly Type II collagen. This collagen takes on an entirely different configuration allowing it to best resist compression forces such as those seen within the disc itself. The Kuslich Application is not directed to healing the annulus by promoting new annular tissue, instead the Kulsich Application is directed to promoting the growth of living natural tissue that mimics the mechanical characteristics of a natural disc.

11. The Belef Application teaches that filling a bladder with inert material within the disc space can also be beneficial by preventing vascularization. It is well understood in the art that non-vascularized tissues undergo a process of "sequestration" in the human body. Without blood supply, the isolated tissue chemically hardens by collagenous cross-linking, dehydrates and shrinks. Tissue growth is only possible in a vascularized environment where living cellular tissue supports a long term matrix in order to maintain continued mechanical support.

12. Nothing in the Belef Application would lead a person of skill in the art of spine surgery to find obvious the concept of using tissue promoting material to stimulate the interconnected growth of fibrous and/or cartilaginous tissue within the disc space in order to stabilize the spinal motion segment by promoting the growth of living natural tissue that mimics the mechanical characteristics of a natural disc.

I declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct.

Executed this 29th day of February, 2008.



Michael Mac Millan, M.D.